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INSIGHTS FOR THE LIFE SCIENCES INDUSTRY

In Silico Studies Shed Light on Immune System

By Jennifer Patterson Lorenzetti, BioIT World

Drawing on the power of a cluster of microcomputers at Ernest Orlando Lawrence Berkeley National Laboratory in Berkeley, Calif., researchers have used computer modelling to point the way to new findings about the presence of an “adaptive control function” in the immune system. The findings not only shed new light on the functioning of the immune system, but also highlight the utility of computer modelling in biological research. Even better than the real thing: computational simulation of movement and chemical changes affecting T-cell signalling molecules in response to the binding of a ligand (antigenic stimulation) on the cell surface.

The in silico experiments, published in the September 25 issue of Science, were led by Arup Chakraborty, PhD, professor of chemical engineering and chemistry at the University of California at Berkeley and a leader in computer modelling for immunological research. His experiments used Berkeley Lab’s Scientific Cluster Support program, which gives researchers access to an array of Linux-based microcomputers connected in parallel to perform as a single system. “From a computational standpoint, we didn't need a major breakthrough,” Chakraborty says ¯ only an opportunity to harness existing computer power.

Chakraborty, together with immunologists Dr. Andrey Shaw of the Washington University in St. Louis School of Medicine (St. Louis, MO) and Michael Dustin, PhD of New York University School of Medicine (New York, NY), predicted the behaviour of T-cells under a variety of conditions ¯ an impossibly cumbersome process in traditional laboratory research.

“We can test out hypotheses very quickly (and) follow every little detail,” Chakraborty says. By looking at the predicted behaviour of T-cells as they are exposed to pathogens, the researchers were able to study the “immunological synapse” ¯ the gap between T-cell and pathogen where the two cells interact.

The model predicted that this synapse is involved in both amplifying weak signals from the pathogen to the T-cell, as well as damping overly strong signals, protecting the cell from death resulting from exposure to the strongest signals. The researchers described this function as an “adaptive controller,” the presence of which was confirmed with studies using transgenic mice.

Chakraborty doubts that researchers would have thought to test for this adaptive controller mechanism without computer models pointing the way. “The computer model found the mechanism; the animals tested it,” he says, adding that the in silico work “provided the insight.” He believes that this sort of experiment points to the opportunities for closer work between traditional biological experimentation and computer modelling.

Although current computing power was sufficient to point to the adaptive controller mechanism, Chakraborty predicts that advances in computer technology will transform these computer models into more reliable facsimiles of biological subjects ¯ what he calls “digital transgenic animals.”

“We need some advances in computer technology; we need to go beyond standard Linux boxes. We need the ability to simulate things in a much more efficient, parallel way,” he says, adding that greater processor speed will also enhance computer modelling use in biological research. Until these improvements come, however, Chakraborty is pleased with the use of these models. They are a "very useful complement" to genetic and biological research, he says.
